Remarks

Responsive to the Office Action mailed 17 March 2010 and with an extension of time to reply of three months, a petition for which with the required fee is filed herewith, the present paper is timely filed on or before 17 September 2010.

By the present paper, claims 1, 7, 8, 10, and 11 are amended, claims 2, 4, 5 and 6 are canceled without prejudice or disclaimer of subject matter therein, and new claims 12 and 13 are presented. Applicants expressly reserve the right to prosecute one or more continuation or divisional applications having claims drawn to canceled subject matter.

Entry of the claim amendments, entry of the new claims, and reconsideration of the Application are respectfully requested.

The Claim Amendments

Claim 1 is amended to recite that the stem cells are embryonic stem cells, incorporating the limitation of claim 2, now cancelled without prejudice. Support for the amendment can be found in the specification at, for example, in the claims as filed.

Claim 1 is further amended to recite that the stem cells are cultured without feeder cells. Support for the amendment can be found in the specification at, for example paragraphs [0033] and [0034], the clear import of paragraph [0034] being that the different embodiment described in paragraph [0033] does not use fibroblast feeder cells.

Claims 7, 8, 10, and 11 are amended to make them consistent with claim 1 from which they depend.

Applicants respectfully submit that the claim amendments do not introduce new matter into the Application.

The New Claims

New claim 12 is drawn to the composition of claim 1 and further including at least one active ingredient selected fro a Markush group. Support for new claim 12 can be found in the specification at, for example, paragraph [0059].

New claim 13 depends from claim 12, and includes the steps of claim 8 plus the step of combining the at least one active ingredient. Support for claim 13 is as for claim 12.

Applicants respectfully submit that new claims 12 and 13 do not introduce new matter into the Application.

Claim Rejections Under 35 U.S.C. § 103

Claims 1 - 11 were rejected as allegedly obvious over United States Patent 6,372,494 ("the '494 patent"). Applicants acknowledge that a prior art reference must be considered for all that it teaches and that a combination of references cannot be defeated simply by arguing against the individual references. However, the Office here relies on a single reference together with (apparently) common knowledge or "common sense" in the art. In this situation, characterization (or mischaracterization) of the teachings of the sole reference can be dispositive. Applicants respectfully disagree with the Office's characterization of what the '494 patent would have actually taught or suggested to the skilled artisan. A specification must be read in its entirety as it would have been read by the skilled artisan of the day. Isolated statements should not be read out of the context of the entire specification. Accordingly, Applicants respectfully traverse.

Applicants were the first to surprisingly discover that compositions containing a combination of two separately obtained "conditioned media" – one obtained by culturing embryonic stem cells (a preferred embodiment) without fibroblast (stromal) feeder cells, the other obtained by culturing a specific type of stromal cell, fibroblasts, in the absence of any other type of cell – are useful in topical skin care products (for example anti-wrinkle compositions). The '494 patent neither taught nor suggested to do what Applicants were the first to do.

At column 10, beginning at line 17, the '494 patent recites (underscore supplied):

> The stromal cells used in the three-dimensional cultures comprise fibroblasts, mesenchymal stem cells, liver reserve cells, neural stem cells, pancreatic stem cells, and/or embryonic stem cells with or without additional cells and/or elements described more fully herein.

As an initial matter, Applicants respectfully submit that the skilled artisan would not credit the statement here (and elsewhere in the '494 patent) that embryonic stem cells are stromal cells.

Fibroblast (stromal) cells are characterized by a Hayflick limit – which limits the proliferation of stromal cells in culture. Hayflick, L. & Moorhead, P.S., *Exp. Cell Res.* Vol. 25, pp. 585- 621 (1961)(human fibroblasts *in vitro* have a finite mitotic lifespan, which is followed by cellular degeneration). Embryonic stem cells are not subject to such a limitation. An embryonic stem cell is "self-renewing (can replicate itself), pluripotent (can form all cell types found in the body) and theoretically is immortal." *See*, http://www.isscr.org/public/glossary.htm#estemcell.

As discussed above, another fundamental difference between stromal cells and embryonic stem cells is that the latter are pluripotent. The Medical Subject Headings published by the National Library of Medicine defines stem cell as "a relatively undifferentiated cell that retains the ability to divide and proliferate throughout life to provide progenitor cells that can differentiate into specialized cells". Stromal cells are understood in the art as non-terminally differentiated (blast) cells and are defined as precursor cells having a "unique fate."

But Applicants do not base their traversal on this ground alone. More important, the recited passage cited by the Office refers to cells used in three dimensional cultures. *If* the skilled artisan *were* to overlook the mischaracterization of embryonic stem cells as stromal cells and read the "and/or" language as urged by the Office, then Applicants respectfully submit that the cited passage cannot teach or suggest culturing embryonic stem cells alone. Rather, in the three dimensional culture system of the '464 patent, the support or "mesh" is first prepared with a growth of stromal cells that then form a "living structure" upon which other cells are grown. *See, e.g.*, '464 patent at column 10, lines 37 – 52. The three dimensional culturing of two different cell types taught by the '494 patent is always sequential. If the embryonic stem cells make-up the "living stromal tissue" that supports the growth of the "other" cells, they are not cultured alone. The "other" cells are cultured on the matrix of the stem cells, or the putative "stromal" embryonic stem cells are simply cultured on themselves.

Furthermore, as Applicants best understand the rejection and the arguments on page 5 concerning the passage cited above and the motivation to modify the teachings

of the reference, the Office appears to construe and apply the teachings of the '464 patent in a mutually exclusive manner.

If the Office considers embryonic stem cells to be stromal cells that can be cultured alone, then the '494 patent does not teach or suggest culturing embryonic stem cells on top of fibroblast feeder cells, and the Office's argument that it would have been obvious to combine conditioned stem cell medium obtained without fibroblast feeder cells with conditioned medium from culturing fibroblasts alone clearly fails.

If, on the other hand, the Office maintains that the '494 patent *does* teach culturing embryonic stem cells on top of fibroblast feeder cells, then the Office's argument for modifying the teachings also fails because modifying the '494 patent to simultaneously culture different cells alone, without feeder cells (as Applicants have done), and later combining the respective conditioned media, instead of culturing sequentially with feeder cells (or living tissue support) as taught by the '464 patent, would eliminate the benefits and advantages described in the '494 patent.

For at least the foregoing reasons, Applicants respectfully submit that the rejection is improper and should be withdrawn.

Conclusion

Based on the foregoing amendments and remarks, Applicants respectfully submit that the claims are now in condition for allowance, which allowance is earnestly solicited. If, in the opinion of the Examiner, a telephone conference would advance prosecution of the Application, the Examiner is invited to telephone the undersigned attorney.

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